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THE WOODLANDS, TX 77381-1160

EXAMINER	
LI, RUIXIANG	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/975,308
Filing Date: October 11, 2001
Appellant(s): FRIDDLE ET AL.

David W. Hibler
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed June 11, 2003 (Paper No. 21).

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is essentially correct, except the asserted utilities for the claimed invention are currently being disputed.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that the claims stand or fall together.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Ji et al., G-protein-coupled receptors, J. Biol. Chem. 273:17299-17302, 1998.

Peer Bork and Eugene V. Koonin, Predicting functions from protein sequences--where are the bottlenecks? Nature Genetics 18:313-318,1998.

Yan et al., Two-amino acid molecular switch in an epithelial morphogen that regulates binding to two distinct receptors. 290: 523-527, 2000.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections—35 U.S.C. § 101

Claims 1-3 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 1-3 are drawn to an isolated expression vector comprising the nucleic acid sequence of SEQ ID NO: 8 or a nucleic acid sequence encoding the amino acid sequence of SEQ ID NO: 9, and a host cell comprising the vector. The claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" context of use for the claimed invention which does not require further research.

The specification asserts that the nucleic acid sequences of the present invention encode a human GPCR (referred as "NGPCR" in the instant case) because the protein encoded by the present nucleic acid sequences has structural motifs

found in the GPCRs family (page 2, lines 1-15). The human GPCR encoded by the present nucleic acids shows sequence similarity to a variety of olfactory receptors (page 2, lines 15-16) and can be detected in a variety of human cells and tissues including those that are not normally associated with olfactory functions (page 2, 16-18; page 5, lines 18-21). However, there is no disclosure of the ligand(s), biological functions, or any physiological significance of the putative GPCR; there is no disclosure of any evidence indicating that the putative GPCR is a truly functional GPCR and is involved in signal transduction pathway involving G-proteins or PPG proteins as being asserted (page 2, lines 2-3); there is no disclosure of any evidence indicating that the nucleic acid sequences of the present invention are expressed at altered levels or forms in any specific, diseased tissue, as compared with the healthy control tissue. Thus, the claimed invention lacks a specific and substantial utility.

The specification asserts a number of utilities for the claimed invention apparently based upon the sequence homology of the protein encoded by the nucleic acid molecules of the present invention: the encoded protein has structural motifs found in the GPCR family. Nonetheless, the specification fails to disclose the degree of homology of the putative GPCR with any particular functional GPCR. The specification even fails to identify the specific seven transmembrane domains—where each domain is located. The state of the art in protein science indicates that it is impossible to predict precisely protein functions solely based upon sequence homology. In view of the diversity of structure and functions of the proteins (Ji et al., G-protein-coupled receptors, *J. Biol. Chem.* 273:17299-17302, 1998), prediction of

function using comparative sequence analysis may lead to the creation and propagation of assignment errors if not performed appropriately (Peer Bork and Eugene V. Koonin, Predicting functions from protein sequences–where are the bottlenecks? *Nature Genetics* 18:313-318,1998). There are putative seven transmembrane molecules, which do not appear to be coupled to a G protein (Ji et al., G-protein-coupled receptors, *J. Biol. Chem.* 273:17299-17302, 1998). In certain cases, a change of two-amino acid residues in a protein results in switching the binding of the protein from one receptor to another (Yan et al., Two-amino acid molecular switch in an epithelial morphogen that regulates binding to two distinct receptors. *Science* 290: 523-527, 2000). Thus, the asserted utilities in the specification based upon the protein sequence homology are not specific and substantial.

The specification asserts that the nucleotide sequences of the present invention can be used to regulate gene expression (page 3, last paragraph-page 4, line 8) and are useful for the identification of protein coding sequence and mapping a unique gene to a particular chromosome (page 4, 2nd paragraph). The specification further asserts utilities of the nucleic acid molecules as hybridization probes for screening libraries, assessing gene expression patterns, particularly using a microarray or high throughput "chip" format (page 10, 3rd paragraph), and identification of novel molecular targets for drug discovery (page 12, 2nd paragraph). The specification further asserts the use of the protein of the present invention in generation of antibodies (page 22, line 9). However, such uses are all considered

research uses only designed to identify a particular function of the present molecules and are not a substantial utility. See, e.g., *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966) wherein a research utility was not considered a "substantial utility." Moreover, such uses are not specific to the instant molecule but applicable to any nucleic acid molecules or proteins.

The specification further asserts that the nucleic acid molecules, proteins, fusion proteins, and antibodies of the present invention "can be useful" for detection of mutants of the protein encoded by the nucleic acid sequences, for screening drugs (page 7, 2nd paragraph), or for diagnosis and treatment of diseases (page 6, 2nd paragraph). These asserted utilities are not specific and substantial because they do not identify or reasonably confirm a "real world" context of use. The specification fails to disclose the biological functions of the present molecules and any diseases that are associated with or can be treated with the molecules of the present invention. Clearly, further research would be required to identify a disease that is associated with the claimed molecules or a disease that can be treated with the claimed molecules. See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

The invention also lacks a well-established utility. A well-established utility is a specific, substantial, and creditable utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. The assertion that the human protein encoded by the nucleic acid molecules comprised in the

claimed expression vectors has the sequence similarity with GPCRs does not endow the claimed invention with a specific and substantial utility. No art of record discloses or suggests any property or activity for the molecules of the present invention such that another non-asserted utility would be well-established for the claimed invention.

In summary, all the asserted uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ at 696.

Claim Rejections—35 U.S.C. § 112, First Paragraph

Claims 1-3 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(11) Response to Argument

A. Do claims 1-3 lack a Patentable Utility?

Beginning at page 4 of the Brief, Appellant argues that the present nucleic acids have utility in forensic analysis, referring to page 4, line 31, page 36, lines 30-31, and page 38, lines 4-5 of the specification. Appellant argues that the present sequences define a coding single nucleotide polymorphism. Specifically, a G/A polymorphism at

position 146 of the nucleic acid sequence of SEQ ID NO: 8, which can lead to a serine or asparagine residue at amino acid position 49 of SEQ ID NO: 9. Appellant further urges that as such a polymorphism is the basis forensic analysis, which is a real world utility, the present sequences must in themselves be useful.

Appellant's argument has been fully considered but is not deemed to be persuasive for the following reasons. The specification merely asserts that the sequences of the present invention are useful as additional DNA markers for restriction fragment length polymorphism (RFLP) analysis and in forensic biology. In view of the definition of the word "forensic": pertaining or applicable to personal injury, murder, and other legal proceedings (Stedman's Medical Dictionary, 27th Edition), it is unclear from the instant disclosure how the asserted polymorphism in SEQ ID NO: 8 is linked to forensic analysis and why the asserted polymorphism in SEQ ID NO: 8 has a specific and substantial utility in forensic analysis, as Appellant argues.

Beginning at the middle of page 4 of the Brief, Appellant argues that the presently described polymorphism, exactly as it was described in the specification as originally filed, is useful in forensic analysis to specifically identify individual members of the human population based upon the presence or absence of the described polymorphism. Appellant argues that in the worst scenario, each of these markers is useful to distinguish 50% of the population. The ability to eliminate 50% of the population from a forensic analysis clearly is real world, practical use.

Appellant's argument has been fully considered but is not deemed to be persuasive because 35 U.S.C.§101 requires disclosure of a specific and substantial utility, or a well-established utility. Such a patentable utility has to be a "real world " context of use which does not require significant further research. In the absence of disclosure of the population that the polymorphic marker distinguishes, such asserted utility is not specific. Since the specification fails to disclose the population that the polymorphic marker distinguishes, significant further research would be required to identify or reasonably confirm a "real word" context of use. Thus, the asserted utility of polymorphism in SEQ ID NO: 8 for forensic analysis is also not considered substantial. In addition, it is unclear from what evidence that Appellant concludes that the asserted marker can distinguish 50% of the population in the worst scenario.

Beginning at the bottom of page 5 of the Brief, Appellant criticizes the Examiner's position that the use of the presently described polymorphic marker in forensic analysis is not specific, but also applied to any other nucleic acids. Appellant submits that the Final Action seems to be confusing the requirement of a specific utility with a unique utility. Appellant argues, citing case law, that the fact that other polymorphic sequences from the human genome have been described does not mean that use of the presently described polymorphic marker for forensic analysis is not specific.

Appellant's arguments have been fully considered but are not deemed to be persuasive for the following reasons. First, Appellant is mischaracterizing the examiner's position regarding the requirements of a specific utility and a unique utility.

There is no dispute on the case law itself. The issue at dispute is what constitutes a specific utility. A specific utility is a utility specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. To satisfy the utility requirement under 35 U.S.C. § 101, a utility does not need to be unique; however, it must be specific. For example, a claim drawn to a polynucleotide whose use is disclosed simply as "a gene probe" or "chromosome marker" would not be considered to be specific in the absence of disclosure of a specific DNA target; a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed. Likewise, the asserted use of the present nucleic acid sequences in forensic analysis in this case is not considered a specific utility in the absence of disclosure of the population that the asserted polymorphic marker distinguishes. In addition, any human nucleic acids may be used to identify human remains or crime scenes. The asserted utility would be applicable to a broad class of nucleic acid molecules.

It is further noted that the patents on batteries, automobile tires, golf balls, and treatments for a variety of human diseases are issued by the USPTO because the invention in each patent has a specific and substantial utility, not simply because the claimed subject matter is related to batteries, automobile tires, golf balls, or disease treatment. For example, a golf ball has a specific feature that makes the ball fly higher and further away as compared with other golf balls; a compound has a particular property that can be used to treat a specific disease, e.g., prostate cancer. It is not the case here.

Beginning at the bottom of page 6 of the Brief, Appellant, citing case law, argues that the present polymorphism is a part of the family of polymorphisms that have a well-established utility and is useful in forensic analysis exactly as it is described in the specification as originally filed, without the need for any further research. Appellant further argue that FDA approval is not a prerequisite for finding a compound useful within the meaning of the patent laws.

Appellant's arguments have been fully considered but are not deemed to be persuasive for the following reasons. First, it is noted that the issue at dispute is about whether the present nucleic acid sequences have a patentable utility in forensic analysis. The present invention is not drawn to a pharmaceutical composition, a drug, or treatment of a specific disease. The Examiner does not dispute the Federal Circuit's holdings. The essential disagreement appears to be the interpretation of what constitutes a patentable utility. A well established utility is a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as DNA or proteins. If this were the case, any nucleic acid sequences would have a well-established utility as a gene probe; the nucleic acid sequences of the of present invention would have a well-established utility in forensic analysis. However, it is not the intention of the statute. As noted immediately above, the asserted utility of the present

sequences in forensic analysis is not specific and substantial because neither the specification nor the art discloses or teaches the population(s) that the asserted polymorphic marker distinguishes whereas identification of such information requires undue experimentation. Thus, the mere disclosure of existence of the A/G polymorphism in the nucleic acid sequence of SEQ ID NO: 8 as originally filed does not necessarily mean that there is a well established utility for the nucleic acid sequences in forensic analysis. If, on the other hand, the specification had clearly the population or subpopulation that the polymorphic marker distinguishes, the nucleic acid sequences and thus the claimed invention would likely have a patentable utility. It is not the case here.

Secondly, while the FDA approval is not a prerequisite for finding a compound useful within the meaning of the patent laws, and the requirement for the utility of the claimed invention is different from the FDA standard for drug approval, 35 U.S.C. §101 does require a specific, substantial, and credible utility, or well-established utility for an invention. Such a utility has to be a "real world " context of use which does not require significant further research. Appellant confuses this requirement with the "further research and development" needed in pharmaceutical composition and drug development. In other words, a patentable utility has to be clearly identified or immediately apparent in the specification, whereas some "further research and development" is permitted in drug development. For example, determining optimal dosages or drug tolerance in human is further research and development, which is acceptable under 35 USC 101 because it is not significant. On the other hand,

determining a specific disease to be treated by a drug constitutes significant further research and development, which is not acceptable under 35 U.S.C. §101.

In the instant case, the specification merely discloses the presence of polymorphism in the nucleic acid sequence of SEQ ID NO: 8. The specification fails to identify the population/subpopulation that the polymorphism distinguishes. Without such information, how can one in the skilled art use the nucleic acid sequences and the claimed invention in a meaningful manner? See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

It is further noted that the instant application was filed on October 11, 2001. No evidence on the specific polymorphisms and the population/subpopulation that the polymorphic marker distinguishes has ever been brought forth in an appropriate form during the prosecution history. It weighs clearly in favorite of Examiner's position that significant further research or undue experimentation is required to identify such information.

At the second paragraph of page 8 of the brief, Appellant argues that two sequences that have over 99% identity at the amino acid level over the entire length of the described sequence are present in GenBank and have been annotated by third party scientists wholly unaffiliated with Appellant as "Homo sapiens gene for seven transmembrane helix receptor" (Accession No. AB065623, Exhibit A) and as a "G-protein coupled receptor" (Accession No. BD144530, Exhibit B), respectively. Appellant

urges that given these two GenBank annotations, there can be no question that those skilled in the art would clearly believe that the Appellant's sequence is a G-protein coupled receptor (GPCR).

Appellant's arguments have been fully considered but are not deemed to be persuasive for the following reasons. First, the key issue at dispute is not a matter of whether the present nucleic acid sequences encode a GPCR; rather, it is a matter of whether the present nucleic acid sequences encode a GPCR with a defined ligand and biological function; it is a matter of whether the present nucleic acid sequences have a specific and substantial utility. The answers to these questions are "No" (see reasons detailed below).

Secondly, the specification merely asserts that the nucleic acid sequences of the present invention encode a human GPCR because the predicted amino acid sequence of the encoded protein has structural motifs found in the GPCR family (Summary of the Inventiona at page 2 of specification). Nowhere does the specification disclose the ligand(s), biological functions, or any physiological significance of the putative GPCR encoded by the present nucleic acid sequences; nowhere does the specification disclose any evidence supporting the assertion that the putative GPCR encoded by the present nucleic acid sequences is a truly functional GPCR and is involved in signal transduction pathway involving G-proteins or PPG proteins as being asserted.

Thirdly, the sequence homology of the predicted amino acid sequence of SEQ ID NO: 9 encoded by the present nucleic acids with the GPCR sequences published in GenBank is insufficient to justify the functions of the human GPCR of the present

invention and to provide the claimed invention a patentable utility. Numerous members of the GPCR family have been cloned so far. However, many of them are still "orphan receptors". The ligands and biological functions of these orphan receptors remain to be identified. Thus, the annotations for the sequences of GenBank do not provide sufficient information for the Examiner to evaluate whether the Genbank sequences represent truly functional GPCRs. It is also noted that the length of the amino acid sequence of the present protein is only about 1/3 of the referred GenBank amino acid sequences. Even if the amino acid sequences in the GenBank were to have a biological function, the protein of the present invention would still not be found to have a specific biological function because a fragment of a protein may not retain the function of the whole protein molecule.

The prior art teaches that it is impossible to predict precisely the functions of protein molecules solely base upon sequence analysis, in view of the diversity of structure and functions of GPCRs (Bork and Eugene V. Koonin, *Nature Genetics* 18:313-318,1998). There were nearly 2000 GPCRs up to 1998 and they are classified into over 100 subfamilies according to sequence homology, ligand structure, and receptor function. There are putative seven transmembrane molecules, which do not appear to be coupled to a G protein (Ji et al., *J. Biol. Chem.* 273:17299-17302, 1998; see beginning of the article). A variety of studies have shown that minor differences in sequence can account for different binding affinities and activities. For example, a change of two-amino acid residues in a protein results in switching the binding of the protein from one receptor to another (Yan et al., *Science* 290: 523-527, 2000).

Furthermore, there is no single well-established utility for the GPCR family due to the great diversity in structures and functions of the GPCR family. Even for a subfamily of the GPCR, the structure and biological activities may vary broadly. Therefore, even the sequence analysis can classify a GPCR into the GPCR family; such an assignment does not render a specific biological function and thus a well-established utility to the GPCR, as is the case here.

Finally, it is noted that the instant application was filed October 11, 2001. No evidence has been brought forth during the prosecution history regarding the ligand(s) and biological activities of the protein of the present invention. It clearly weighs in favorite of the Examiner's position that the functions of the protein encoded by the nucleic acid sequences of present invention remain elusive.

Beginning at bottom of page 8 of the Brief, Appellant criticizes the rejection's use of Bork and Koonin (*Nature Genetics* 18:313-318,1998), Ji et al. (*J. Biol. Chem.* 273:17299-17302, 1998), and Yan et al. (*Science* 290:523-527, 2000). Appellant argues that these articles fail to support the lack of utility of the presently claimed invention.

Appellant urges that the Bork and Koonin article is hardly indicative of a high level of uncertainty in assigning function based on sequence. This has been fully considered but is not deemed to be persuasive because it ignores the overall teachings of Bork and Koonin article. Bork and Koonin's remarks clearly indicate that the potential importance of sequence analysis in extracting functional signal. However, Bork and Koonin do not teach, in any means, that sequence analysis alone can define the biological functions. In fact, Bork and Koonin clearly teach that the exponential growth of

sequence data does not necessarily lead to an increase in knowledge about the functions of genes and their products and that prediction of function using comparative sequence analysis may lead to the creation and propagation of assignment errors if not performed appropriately (Abstract). Bork and Koonin further teach that many proteins are multifunctional, assignment of a single function, which is still common in genome progects, results in loss of information and outright errors (Table 2). As stated in the Office Action (Paper No. 12), while sequence analysis is important, the information provided or "predicted" based upon sequence homology can only be used as guidance in determining functions or activities of a molecule by experiments. Any functions predicted based upon the sequence homology will have to be confirmed ultimately by direct experimentation.

Appellant urges that an exact quote from Ji et al. completely undermines the question of asserted utility based upon protein homology: "a substantial degree of amino acid homology is found between members of a particular subfamily, but comparisons between subfamilies show significantly less or no similarity". Appellant further urges that homology with members of a G-protein coupled receptor is indicative that the particular sequence is in fact a member of that subfamily. This has been fully considered but is not deemed to be persuasive for the following reasons. First, the Examiner notes that the critical issue at dispute is not a matter of whether the present nucleic acids encode a GPCR; rather, it is a matter of whether the GPCR encoded by present nucleic acids have defined biological functions and have a patentable utility. The cited statement simply indicates that a substancial degree of amino acid homology

is found among members of a particular subfamily. However, two sequences sharing certain degree homology do not necessarily have the same functions. Secondly, the specification merely discloses that the nucleic acid sequences of the present invention encode a putative human G-protein coupled receptor (see, e.g., Summary of the Invention at page 2). Nowhere in the specification specifies a functional G-protein coupled receptor with which the protein encoded by the present nucleic acid sequences share sequence homology, and the degree of homology. Moreover, Ji et al. clearly teach that there are putative seven transmembrane molecules, which do not appear to be coupled to a G protein (page 17299, third paragraph of left column, Ji et al.). Even if the protein encoded by the present nucleic acid sequences were able to be placed, based upon sequence homology, within the GPCR family, there would still not be a patentable utility for the claimed invention because there is no common use and thus there is no well established utility for the diversified GPCR family. In this regard, it is noted that there are nearly 2000 G-protein coupled receptors up to 1998, and there are over 100 subfamilies classified according to the sequence homology, ligand structure and receptor funcions (see, e.g., beginning of the article of Ji et al.).

Appellant argues that the paper of Yan et al. cites only one example, two isoforms of the anhidrotic ectodermal dysplasia (EDA) gene, where a two amino acid change conforms one isoform (EDA-A1) into the second isoform (EDA-A2) and does not suggest a high level of uncertainty in assigning function based on sequence, and thus does not support the lack of utility. Specifically, Appellant argues that the different receptors bound by the two isofroms of ectodysplasin are related and that EDA-A2

receptor was correctly identified as a member of the tumor necrosis factor receptor superfamily based upon solely on sequence similarity.

This has been fully considered but is not deemed to be persuasive for the following reasons. First, the paper of Yan et al., while citing only one example, clearly demonstrates that the unpredictability of the functions of proteins solely based upon sequence homology. While the two receptors bound by the two isofroms of ectodysplasin are related, i.e., belonging to the TNFR superfamily, they clearly have different activities (See, e.g., page 524, column 3) and are distinct receptors. Even the title of the paper clearly states that the two receptors bound by the two isoforms are distinct. Secondly, while the EDA-A2 receptor was initially identified as a member of the TNFR superfamily solely based on sequence similarity, as applicants argued, the biological functions of the receptor were not identified. In fact, Yan et al. performed undue experimentation as described in the paper to define the ligand and biological activies of the EDA-A2 receptor. As taught by Yan et al., members of the TNFR superfamily are involved in a number of physiological and pathological response by activating a wide variety of intracellular signaling pathways (beginning of page 523). The EDA-A2 receptor (XEDAR) fails to bind many known ligands of the TNFsuperfamily (1st column of page 524). Therefore, even if sequence analysis could assign a given protein to a protein family, the protein would not necessarily possess the same functions of a member of the family. Consequently, the protein does not have a substantial utiltiy because the biological function or activity is not defined and determining such a biological function of the protein would require significant further research, as

demonstrated by Yan et al., which is not allowed under 35 U.S.C.§ 101. It is the case here.

Beginning at the bottom of page 9 of the Brief, Appellant argues that as 60% of the pharmaceutical products currently being marked by the entire industry target G-protein coupled receptors, a preponderance of the evidence clearly weighs in favor of Appellant's assertion that the skilled artisan would readily recognize that the presently described sequences have a specific, credible, and well-established utility, for example in tracking gene expression, particularly using a gene chip. Appellant further argues that such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents and industrial success.

This has been fully considered but is not deemed to be persuasive for the following reasons. First, commercial success is not an indication of patentability and the commercial value does not simply render the claimed invention a specific and substantial utility. This is because many products may be commercially successful due to reasons unrelated to the use of the products such as fads or clever commercial advertising. For example, a pharmaceutical company may wish to purchase a putative GPCR on the chance that it may turn out to be a drug target in the future, even though determining such possibility requires substantial further experimentation. However, such substantial further experiment is not acceptable for patentable utility. In addition, substantial further experiment may have already been done on some of the GPCRs

mentioned by Appellant in the Brief and specific functions may have already been known. This is not the case here.

Secondly, the Examiner would like to draw the Board's attention to the definition of the terms "a gene chip" and " a micro array" mentioned in the Brief and in the instant specification by the Appellant. A gene chip is a customized device in biomedicine that allows researchers to detect, simultaneously, the presence and activity patterns of tens of thousands of DNA sequences in pieces of genetic material. A micro array can be used by researchers to describe the genetic malfunction associated with a disease, detect the presence of the disease in a particular patient, calculate a patient's genetic predisposition to that disease or identify the medicines likely to be most effective in treating a particular patient with the disease.

The specification merely discloses that the present NGPCR is expressed in a variety of human cells and tissues (page 5, lines 18-21) and has not established that the nucleic acid sequences of the present invention are expressed at altered levels or forms in a specific diseased tissue as compared with the corresponding healthy tissue. If the present nucleic acid molecules were in a microarray and a compound caused decreased expression of the nucleic acids, what would that mean to the skilled artisan? Is it a potential drug, or would administering the compound be likely to acerbate an unspecified disease? If it had been disclosed that the present nucleic acids are expressed at a higher level in a particular diseased tissue as compared with the corresponding healthy tissue, the skilled artisan would know that a compound that decreased expression of the nucleic acid molecules is a good drug candidate that

targets the disease. It is not the case here. In addition, the present nucleic acid molecules may very well be expressed at equivalent levels in healthy tissues. If that were the case, then the compound would not be a good drug candidate. The present nucleic acid molecules may also very well be expressed at a lower level in a particular diseased tissue as compared to the corresponding healthy tissue; a compound that decreased expression of the claimed polynucleotides would *not* be a good potential drug. The Examiner notes that evidence of a differential expression might serve as a basis for use of a nucleic acid molecule as a diagnostic for a disease. However, in the absence of any disclosed relationship between the present nucleic acid molecules (or proteins encoded by the nucleic acids) and any diseases or disorders, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ at 696. Thus, the disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

Finally, the issued U.S. Patents related to DNA chips merely show that the technology itself is important and useful; they do not show that claimed invention has a patentable utility. There is no doubt that a gene chip (or DNA chips) is a valuable tool in gene expression monitoring and drug discovery. However, the claims are not drawn to the technique, rather to an expression vector comprising a nucleic acid molecule, which has not been disclosed as being associated with any particular diseases or conditions by its being expressed at an altered level or form in a specific diseased tissue as

compared to the corresponding healthy tissue. Any such uncharacterized nucleic acid molecules could be added to a micro array. However, such a use of the uncharacterized nucleic acid molecules would have provided no more valuable information than the use of any other unidentified nucleic acids. Thus, this asserted utility is not specific. Determining the relationship between the present nucleic acid molecules and any specific diseases or disorders would require significant further research. Therefore, this asserted utility is also not substantial.

Beginning at the 2nd paragraph of page 11 of the Brief, Appellant criticizes the statement in the final action "since the disclosure does not reveal any activity/functions of the nucleotide sequence or the protein encoded by the nucleotide sequence, one skilled in the art would not know how to use the claimed invention" and argues that expression profiling does not require a knowledge of the function of the particular nucleic acid on the chip—rather the gene chip indicates which DNA fragments are expressed at greater or less levels in two or more particular tissue types.

This has been fully considered but is not deemed to be persuasive for the following reasons. First, Appellant is mischaracterizing the Examiner's position. A specification can meet the legal requirements of utility and enablement for an invention as long as the specification discloses a specific and substantial asserted utility or a well-established utility for the claimed invention. A hypothetical example may serve to clarify. For example, a hypothetical specification discloses that a nucleic acid is expressed in colon cancer but not expressed in healthy colon tissue. The hypothetical specification

does not disclose the biological activity of the polypeptide encoded by the nucleic acid. The nucleic acid in the hypothetical example would not be rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as it has a specific and substantial utility and is enabled as a colon cancer marker.

However, it is not the case here. The instant specification merely discloses that the nucleic acid sequences of the present invention encode a putative human G-protein coupled receptors (see page 2, Summary of the Invention) and can be detected in a variety of human cells and tissues (page 5, lines 18-21). There is no disclosure that the present nucleic acids are expressed at altered levels or forms in any specific, diseased tissue. It is noted that the instant application was filed October 11, 2001. No evidence has been brought forth during the prosecution history regarding the expression levels in diseased or healthy tissue; no evidence has been brought forth on the biological activities of the protein encoded by the present nucleic acids. Since the specification fails to discloses nucleic acid molecules as being associated with any particular diseases or conditions by its being expressed at an altered level or form in a specific diseased tissue as compared to the corresponding healthy tissue, as discussed above, what meaningful results could one possibly obtain even one can carry out the assay using a gene chip?

Furthermore, if Appellant intends to argue that the present nucleic acid sequences can be used in a gene chip to determine their differential expression associated with a certain disease, it is analogous to argue that the nucleic acid

sequences of the present invention lack a patentable utility in its current available form because establishment of the usefulness requires further research.

At page 11, the 3rd paragraph of the Brief, Appellant argues that persons of skilled in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of human genomic data and that the usefulness of the nucleic acid molecules of the present invention is substantial and credible and well established. This has been fully considered but is not deemed to be persuasive because while human genomic data have both scientific and commercial value, neither the commercial success related to human genomic project nor the publications cited by the Appellant shows a patentable utility for the present invention.

Beginning at page 11, the 4th paragraph of the Brief, Appellant argues that the present polynucleotide sequences have a specific utility in mapping the sequences to a specific region of a human chromosome and provide biologically validated empirical data that specifically define that portion of the corresponding genomic locus that actually encodes exon sequence.

This has been fully considered but is not deemed to be persuasive because such a utility is considered a research utility only designed to identify a particular function of the nucleic acid sequences and is not a substantial utility. See, e.g., *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966) wherein a research utility was not considered a "substantial utility." Moreover, such a utility is not specific to the instant

nucleic acid molecules, rather applicable to any polynucleotide sequences encoding proteins. Thus, while the Examiner agrees with the Appellant on the scientific value of the present polynucleotide sequences and on the significance of expressed sequence information in structural analysis of genomic data, such a use of the polynucleotide sequences in gene mapping does not represent a specific and substantial utility. Moreover, the exhibit and the publication cited by the Appellant merely show that the significance of expressed sequences in the structural analysis of genomic data; they do not show that the present polynucleotide sequences have a patentable utility.

Beginning at the bottom of page 12 of the Brief, Appellant summarizes case law on the utility requirement. Citing case law, Appellant urges that the present claims clearly meet the requirement of 35 U.S.C. §101. The essential disagreement appears to be the interpretation of what constitutes a specific, substantial and credible utility, and on the statement "(t)o violate §101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 USPQ2d 1401 (Fed. Cir. 1992).

Appellant's arguments have been fully considered but are not deemed to be persuasive for the following reasons. First, the statement quoted from the device case law indicates that a rejection under 35 U.S.C. § 101 *for lack of operability* can be overcome by a showing of actual use or commercial success. The instant claims are drawn to an expression vector comprising a nucleic acid sequence encoding the amino acid sequence of SEQ ID NO: 9 and a host cell comprising the expression vector, not a

device; the instant rejection under 35U.S.C. §101 is not directed to inoperativeness of a device, rather to a lack of patentable utility of the expression vector or a host cell comprising the vector; and the instant issue is whether the asserted utilities meet the three-pronged test for a patentable utility. Secondly, since the specification fails to disclose a specific, substantial utility or a well-established utility, the present invention do not satisfy the utility requirement of 35 U.S.C. §101. Merely citing case laws on the utility requirement does not render a patentable utility for the present invention. While "anything under the sun that is made by man" is patentable, it does not necessarily mean the present invention is patentable. In fact, the present invention is not patentable due to lack of a patentable utility.

Finally, beginning at bottom of page 13 of the Brief, Appellant challenges the legality of the Patent Examination Utility Guidelines and the validity of issued US patents. It is noted that an Examiner has no authority to comment on the legality of the Guidelines and the validity of US Patents.

Appellant concludes this section by urging that the rejection of claims 1-3 under 35 U.S.C. § 101 must be overruled. The Examiner believes that the rejections should be sustained for the reasons set forth above.

B. Are Claims 1-3 Unusable Due to a lack of Patentable Utility?

Claims 1-3 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial

asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

As Appellant indicates at page 15 of the Brief, a rejection under § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under § 101. Applicants submit that as claims 1-3 have been shown to have a specific, substantial and credible utility, the present rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, cannot stand. The Examiner believes that the rejection should be sustained for the reasons set forth above.

Therefore, for reasons set forth above, Appellant's arguments and exhibits have been fully and carefully considered, but are not considered sufficient to rebut the prima facie case of lack of utility and enablement.

For the above reasons, it is believed that the rejection should be sustained.

Respectfully submitted,

Ruixiang Li, Ph.D.
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Brenda Brumback
BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Conferees
Brenda Brumback, Ph.D.
SPE, Art Unit 1647

Christina Chan, Ph.D.
SPE, Art Unit 1644